
MEETING REPORT

Report on the Tenth Annual Scientific Meeting of the UK Drug Utilisation Research Group Friday 11 December 1998 The Royal Society of Medicine, London

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THE USE AND ABUSE OF ANTIBIOTICS

The theme for the morning session was 'Evidence-based Prescribing' and the Chairman was Dr John J. Ferguson, Honorary Secretary, UK DURG.

The first speaker was Lord Soulsby, of Swaffham Prior, Chairman of the House of Lords Select Committee on Science and Technology on 'Resistance to Antimicrobials'. He described antimicrobial resistance as a worldwide problem growing in size since it was first discovered in the 1950s. He outlined the mechanisms of bacterial resistance and the way in which habitat pressures favour resistant bacterial populations. Resistance levels vary according to the antibiotic but are rising in all. He listed the antibiotics under threat and the diseases which may become untreatable as a result. Even birds and reptiles have been colonized by antibiotic resistant flora. Spread of resistance is rapid as a result of air travel. Lord Soulsby cited complacency as a major obstacle blocking effective action to counter resistance. The main cause of resistance in human pathogens is the unnecessary prescribing of antibiotics in medicine, particularly for upper respiratory infections which were usually viral. However, veterinary surgeons also need to be concerned at the growth of shared resistance both in animal pathogens and commensal flora. The use of antimicrobials in agriculture should be restricted to veterinary treatment and the use of certain antibiotics used or proposed to be used in man as

growth promoters in animal feeds should cease altogether. Farmers and their families may share the antibiotic resistant commensal organisms of their animals. Lord Soulsby regretted the failure of action by the authorities to implement the Swann Report of thirty years ago on this subject. He concluded by calling for a single multidisciplinary committee at both British and European levels to oversee antibiotic use, and the production of guidelines and regulations to ensure their adherence.

THE WORK OF THE UK COCHRANE CENTRE

Dr Philip Alderson, of the UK Cochrane Centre, Oxford explained the functions of the Cochrane Collaboration in avoiding unnecessary research duplication, reducing bias, ensuring currency, relevance, easy access and quality assurance. The key elements were the Cochrane Review Groups, now about fifty in number. The Cochrane Library database now includes over 190,000 trial reports, 33,000 controlled trials from Medline and 20,000 from Embase. Many general and specialist journals have been hand-searched. Registration of ongoing trials and as yet unpublished trials is also encouraged.

The second function of the UK Cochrane Centre is the training of personnel in the preparation of review. Five hundred reviews are now completed and in the Cochrane Library. In terms of quality assurance, the avoidance or reduction of publication bias is paramount, and good progress has been

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made compared with a random sample of reviews in peer-reviewed journals.

Dr Alderson concluded by stating that the Cochrane Reviews are now being more widely used by UK and Commonwealth authorities and by researchers applying for funding for projects which a Cochrane Review has recommended for further investigation. The NHS Research and Development Programme and the Medical Research Council are now using Cochrane Reviews to help prioritize research applications.

COST-EFFECTIVE PRESCRIBING

Professor Alain Li Wan Po, Professor of Clinical Pharmaceutics, University of Aston, Birmingham first described the pressures on prescribers, citing the ageing population, advances in diagnostic technology and the demand of equalizing access of treatment. This has led to the problem of reconciling limited resources with limitless demand, and hence making cost-effective prescribing essential to the survival of the NHS. Defining cost-effective prescribing as a treatment producing an effect worth paying for, Professor Li Wan Po outlined some of the problems. First, the conflict between what is beneficial for the individual and for society. The problem of individual demand for treatment is that under a publicly funded national health system the individual does not shoulder the full costs and therefore tends to make excessive demands. Additionally, the general practitioner is not legally obliged to take cost into account. Further advertising to the GP fuels prescribing. Next there is a serious lack of systematic reviews of evidence on cost-effectiveness, which are only beginning to appear. Surrogate markers of cost-effectiveness and observational studies are unsatisfactory, for example a recent randomized-controlled trial on HRT in the *Journal of the American Medical Association* suggests that the treatment does not reduce cardiovascular risk. Finally assessing cost-effectiveness is difficult due to indirect costs, including adverse drug reactions, poor data on hospitalization and absence from employment. The speaker concluded by taking antidepressant treatment as an example, where the newer antidepressants (SSRIs) are widely perceived as having a lower incidence of adverse drug reactions. This perception is false — the ADRs are equally present, but different in the SSRIs and the TCAs.

THE DEVELOPMENT OF NEW DRUGS

Professor Trevor Jones, Director General of the Association of the British Pharmaceutical Industry emphasized the drug industry's investment in research and development and its contribution to the national budget. He reminded members that the cost of Research and Development of new drugs is approximately \$600 million per entity, with a 10–12 year gestation. He emphasized the need for supply and intellectual freedom for the industry's research scientists in discovering new potential treatments and the need thereafter for management to develop their discoveries. This involved not only screening of potential compounds for biological activity as in the past, but also, researching known side-effects of existing treatments as potentials for other treatment — e.g. lamotrigine, the anticonvulsant, showed promise as a potential analgesic. More exciting still was the prospect offered by the new science of genomics, e.g. sequencing bacterial genomes, searching for potential new antibiotics. By the year 2000, up to 20,000 compounds per day will be screened. Professor Jones said that we have travelled from *in vivo* to *in vitro* to *in silico*. The future looked very exciting, with apparently limitless prospects for drug development including the promise of specific treatment for AIDS and the prospect of screening individual patients serologically, and tailoring combination treatment to the individual. Finally, he strongly supported the interests of the individual versus society, especially in the context of making available genomic information on patients.

A lively general discussion followed on the morning's presentations.

The afternoon session was devoted to research presentations from members, and was chaired by the Chairman of UK DURG, Professor John Feely.

PRESCRIBING BUDGETS FOR PRIMARY CARE GROUPS (PCGs) — IMPLEMENTING THE GUIDELINES

Mr Darrin Baines of the University of Birmingham described the challenges for PCGs as managing budgets, evaluating new drugs, making savings and promoting rational prescribing. He asked whether rationing was inevitable and whether primary care physicians would be happy to undertake this task. He argued that fundholding had achieved limited

successes and resulted in short-term savings only. Regarding plans for PCG budgets, Mr Baines asked whether incentives were required, whether budgets should be set mechanistically or by negotiation, whether constraints should be 'soft' or 'hard', and whether equity or opportunism should prevail. Moreover, decisions had to be made as to whether budgets were to be global or at the therapeutic group level. Finally, he advocated the use of several strategies in setting prescribing budgets for PCGs, a recognition of the limited scope for financial savings, suggesting that, in the longer-term, budgets may be replaced by local formularies and guidelines in managing PCG expenditure.

ACHIEVING CONCORDANCE IN PRACTICE

Dr Jon Dowell of the University of Dundee summarized the Royal Pharmaceutical Society's suggestion that 'concordance' implied the patient's beliefs were accepted by the doctor, the doctor's beliefs by the patient and agreement was reached by both on plans for medication. He described a study in which 24 adult non-compliant patients with serious chronic illness were offered up to four 20-minute consultations based on the therapeutic decision model (TDM) employing a highly patient-centred approach. Prompt-cards were used to help reveal misunderstandings about illness or treatment, lack of motivation and confrontational attitudes, consultations concluded with negotiation of the level of control by the patient and agreement of therapeutic goals. On occasion including the 'no treatment' option. The results showed that it was a satisfying, effective and ethical way to practice. Doctors thought the intervention useful for 22 of the 24 patients and noted clinical improvement in 15. Five key stages were evident from the study:

1. A break from the usual clinical relationship had to be signalled.
2. Patients' understanding of their illness and treatment was explored.
3. Experience of medication use was explored.
4. Misunderstandings, poor motivation or barriers to accepting treatment were discussed.
5. Treatment goals, treatment use and the level of patient control were agreed.

The complexity and time-consuming nature of the process make widespread implementation

difficult. The need for training and appropriate patient selection was emphasized.

PIONEERING PHARMACEUTICAL NEEDS ASSESSMENT IN PRIMARY CARE

Dr Sharon Williams of the University of Aberdeen described how a multipartner general practice used a needs assessment to prioritize pharmaceutical services to be provided by a practice based pharmacist. All client groups (patients, GPs, community and hospital pharmacists, nurses and administrative staff) participated in the assessment which was based on the techniques of 'gap analysis', 'nominal group technique' and 'rapid participatory appraisal'. Areas of 'need' identified by the client groups reflected their roles but there were areas of accord. By consensus it was agreed that the services to be initially provided should be: a patient medication education clinic, the development and implementation of a prescribing policy for lipid management and computer housekeeping. The assessment provided both a formal mechanism for patients to have their say in the service they receive and a baseline to aid the prioritization of future service provision.

EVIDENCE-BASED PRESCRIBING—WHAT EVIDENCE AFFECTS PRESCRIBING?

Mr Martin Jenkins of the Prescription Pricing Authority, Newcastle-upon-Tyne, set out to evaluate which evidence affects GP prescribing and to quantify the effect, using the Prescription Pricing Authority database. He showed temporally based histograms showing the numbers of prescriptions issued per quarter for England and Wales, for minocycline, selegiline, pancreatin and third-generation oral contraceptives. For the first three, a dramatic fall in prescription issue followed the publication of a paper describing adverse drug reactions (ADRs), the first two in the *British Medical Journal*, the third in the *Lancet*. For the fourth item, the stimulus to reduction in issue of prescriptions was the publication of 'dear doctor' letter by the Committee on Safety of Medicines, together with much media coverage of the increased risks from the progestogen in the third level OCs. The possible relationship between the number of ADRs reported and the change in patient years treatment had been examined to see if

there was a quantifiable relationship. Mr Jenkins concluded that reports on ADRs in relatively few patients caused a disproportionate response, that the commonly-read journals are by far the most powerful, and that the media have a large effect both on patient demand and on doctors' attitudes. His research team is continuing to test this further, particularly to investigate whether the most effective papers in changing prescribing habits are also scientifically good papers.

TREATED ASTHMA IN GENERAL PRACTICE — PATIENT BASED PRESCRIBING ANALYSIS

Dr Martin Frischer of the University of Keele demonstrated the limitations of aggregated prescribing data (e.g. PACT) as compared with patient-based prescribing data, contained in the General Practice Research Database (GPRD). He noted that the GPRD has not yet been extensively used in drug utilization research in the UK, although it has the potential to address a wide range of issues arising from medicines usage. One example, is the role of the British Thoracic Society (BTS) guidelines in treatment asthma in general practice. As an indicator of appropriate treatment, the use of the leukotriene receptor antagonist montelukast was investigated. The prevalence of treated asthma was recorded, the severity of asthma and BTS stage of treatment was noted, the relationship between preventer:reliever ratio and hospital admissions was measured and switching between types of medication was noted. Results indicated that the prevalence of treated asthma was 5.9% of whom one fifth might be appropriate first line candidates for montelukast, based on severity and current medication. While previous studies of the preventer:reliever ratio in asthma have led to

conflicting results, analysis of individual patients' ratios showed that higher ratios were associated with lower hospitalization (adjusted odds ratio, 0.87–95% CL 0.73 to 0.98). Dr Frischer suggested that GPRD could complement PACT data by adding information on patient characteristics and diagnoses, thus allowing issues of appropriateness and effectiveness to be addressed.

SAFETY PROFILES AND PRIMARY CARE PRESCRIBING OF NSAIDs 1989–1998 NORTHERN REGION

Mr Philip Young, Regional Drug and Therapeutics Centre, Newcastle-upon-Tyne cited the well-known adverse drug reactions to NSAIDs which accounted for 3.5% of NHS prescriptions in 1997–98. Six individual NSAIDs account for the majority of prescriptions and for about 25% of all adverse drug reactions reported to the Committee on Safety of Medicines. His study aimed to review NSAID prescribing in primary care, to identify the NSAIDs with greatest risk and using level 3 PACT and PACTLINE from the Prescription Pricing Authority, to show variation in NSAID prescribing between the health authorities of the former Northern region. Separating NSAIDs into three groups — toxic oral preparations, safer oral preparations and topical preparations, he showed that in the decade surveyed, prescribing of all NSAIDs had risen by 21%, but prescribing of toxic NSAIDs had fallen by 46%. Use of safer NSAIDs had risen accordingly by 54% while the use of the illogical topical NSAIDs had increased by only 7%. He concluded that as a result of information provided to prescribers, safer NSAIDs were now more often used than previously.